1 522 657

PATENT SPECIFICATION (11) 1 522 657

(21) Application No. 47071/75 (22) Filed 14 Nov. 1975
(31) Convention Application No. 524 587
(32) Filed 18 Nov. 1974
(31) Convention Application No. 620 989
(32) Filed 9 Oct. 1975 in
(33) United States of America (US)
(44) Complete Specification published 23 Aug. 1978
(51) INT CL² C07D 249/08, 317/12
(52) Index at acceptance
C2C 1228 1450 1492 1510 215 220 222 226 22X 22Y 246 247 250 252 253 254 25Y 28X 29X 29Y 30Y 311 313 314 315 31Y 326 332 338 364 36Y 43X 621 624 62Y 662 666 669 681 697 69Y 708 73Y 77Y 791 79Y MM NR WJ ZD

(19)

(54) TRIAZOLE DERIVATIVES AND THEIR USE AS ANTIMICROBIAL AND PLANT-GROWTH REGULATING AGENTS

PATENTS ACT 1949

SPECIFICATION NO 1522657

The following amendments were allowed under Section 29 on 12 December 1980:

Page 2, line 2, Page 19, line 9, *delete* , naphthyl or fluorenyl *insert* or naphthyl

Page 5, Table 1, first line, *delete* 2-fluorenyl H base O

Page 14, *delete* line 17

Page 15, *delete* lines 37 and 38

Page 20, lines 32 and 34, *for* 21 *read* 19

THE PATENT OFFICE
19 January 1981

Bas 80642/8

z

wherein:
Z is an alkylene group of the formula:

$$-CH_2-CH_2-,\ -CH_2-CH_2-CH_2-,$$

$$-CH(H_3C)-CH(CH_3)-$$

or

$$-CH_2-CH(\text{alkyl})-$$

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(19)

(54) TRIAZOLE DERIVATIVES AND THEIR USE AS ANTIMICROBIAL AND PLANT-GROWTH REGULATING AGENTS

(71) We, JANSSEN PHARMACEUTICA N.V., a Belgian Body Corporate, of Turnhoutsebaan 30, Beerse, Belgium, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

The present invention relates to certain 1-(β-aryl)ethyl-1H-1,2,4-triazole ketals useful for their antimicrobial and plant-growth regulating activities.

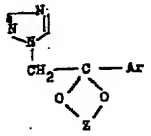
United States Patent Specification No. 3,575,999 describes 1-(β-aryl)ethyl-imidazole ketals having antibacterial and antifungal properties.

In the prior art a number of other triazole derivatives are also described, some of which are described as fungicides or growth regulators.

The compounds of this invention differ from the triazole derivatives of the prior art by the nature of the side chain which is attached to the triazole nitrogen atom.

It is believed that the closest prior art triazole derivatives are described in the following reference: French Patent Specification No. 2.200.012 (Derwent Week V25 — Pharm. p. 7.)

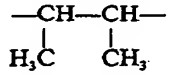
The present invention provides 1H-1,2,4-triazole derivatives having the general formula:



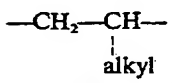
(I)

wherein:
Z is an alkylene group of the formula:

$$-CH_2-CH_2-,\ -CH_2-CH_2-CH_2-,$$



or



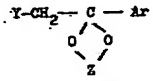
SPECIFICATION AMENDED - SEE ATTACHED SLIP

wherein said alkyl group has from 1 to 10 carbon atoms; and Ar is a phenyl, thienyl, halothienyl, naphthyl or fluorenyl group, or a substituted phenyl group having from 1 to 3 substituents which are independently a halogen atom, a lower-alkyl, loweralkyloxy, cyano or nitro group.

The therapeutically active acid addition salts of the compound of formula (I) are also included in the scope of this invention.

As used in the foregoing definition of the group Z, the term "alkyl" covers straight and branched chain hydrocarbon groups having from 1 to 10 carbon atoms, such as, methyl, ethyl, 1-methylethyl, propyl, 1,1-dimethylethyl, butyl, pentyl, hexyl, heptyl, octyl or decyl; as used herein the term "loweralkyl" refers to straight or branched chain saturated hydrocarbon groups having from 1 to 6 carbon atoms, such as methyl, ethyl, propyl, 1-methylethyl, butyl, 1,1-dimethylethyl, pentyl or hexyl; and the term "halogen" is generic to halogen atoms of atomic weight less than 127; i.e., fluorine, chlorine, bromine and iodine.

The ketals of formula (I) may be readily obtained by reaction 1H-1,2,4-triazole (II), previously converted into a metal salt thereof, such as, for example, by treatment with an alkali metal alkoxide, preferably sodium methoxide, with a halide of formula (III)

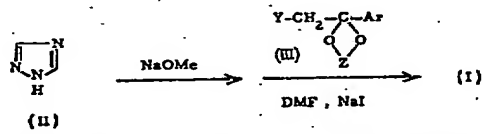


(III)

wherein Ar and Z are as previously defined and Y is a halogen atom, preferably bromine. The reaction of the metal salt of 1H-1,2,4-triazole (II) with compound (III) is preferably carried out in an appropriate polar reaction-inert organic solvent, such as N,N-dimethylformamide, N,N-dimethylacetamide, acetonitrile or benzonitrile. Such solvents may be used in combination with other reaction-inert organic solvents, such as, benzene, methylbenzene or dimethylbenzene. When Y represents a bromine or chlorine atom, the addition of an alkali metal iodide, such as sodium- or potassium iodide is appropriate. Elevated temperatures are appropriate to enhance the rate of the reaction and most preferably the reaction is carried out at the reflux temperature of the reaction mixture.

The resulting ketal of formula (I) may then be isolated from the reaction mixture by conventional means and, if desired, further purified according to common purification procedures such as crystallization, extraction, trituration or chromatography.

The foregoing procedure is further illustrated by the following reaction scheme:



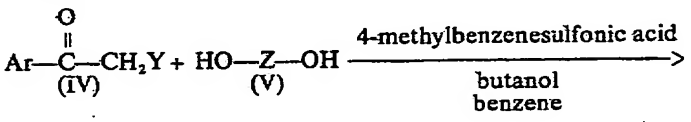
The thus-obtained compounds of formula (I), in base form, may be converted into their therapeutically useful acid addition salts by reaction with an appropriate acid, as, for example, an inorganic acid such as a hydrohalic acid, i.e., hydrochloric, hydrobromic or hydroiodic acid; sulfuric, nitric or thiocyanic acid; a phosphoric acid; an organic acid such as acetic, propionic, hydroxyacetic, α-hydroxypropionic, 2-oxopropionic, ethanedioic, propanedioic, 1,4-butanedioic, (Z)-2-butenedioic, (E)-2-butenedioic, 2-hydroxy-1,4-butanedioic, 2,3-dihydroxy-1,4-butanedioic, 2-hydroxy-1,2,3-propanetricarboxylic, benzoic, 3-phenylpropenoic, α-hydroxybenzeneacetic, methanesulfonic, ethanesulfonic, hydroxyethanesulfonic, 4-methylbenzenesulfonic, α-hydroxybenzoic, 4-amino-2-hydroxybenzoic, 2-phenoxybenzoic or 2-acetoxybenzoic acid. The salts may be converted to the corresponding free bases in the usual manner, e.g., by reaction with alkali such as sodium or potassium hydroxide.

The starting compounds of formula (III), a number of which are known compounds, may be prepared according to known procedures. Such compounds wherein Z is an alkylene group of the formula:

$$-CH_2-CH_2-,\ -CH(CH_3)-CH_2-,$$
$$-CH(CH_3)-CH(CH_3)- \text{ or } -CH_2-CH_2-CH_2-$$

and methods of preparing them are described in United States Patent Specification No. 3,575,999. In general, the compounds of formula (III) may be prepared by the ketalization of an appropriate ketone of formula (IV) wherein Ar and Y are as previously defined, with an appropriate diol of formula (V) following known ketalization procedures as are described in the literature [see e.g. Synthesis, 1974 (1), 23].

In a preferred method both reactants are refluxed together for several hours with azeotropic water removal in an appropriate organic solvent, preferably in the presence of a simple alcohol, such as ethanol, propanol, butanol or pentanol, and in the presence of an appropriate strong acid such as 4-methylbenzenesulfonic acid. Suitable organic solvents which may be used therefore include, for example, aromatic hydrocarbons such as benzene, methylbenzene or dimethylbenzene and saturated hydrocarbons, such as cyclohexane.



(IV) (V) (III)

The ketones of formula (IV) are generally known and may be prepared by methods which are known to those skilled in the art.

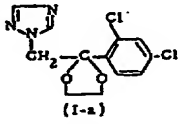
From formula (I) it is evident that several of the compounds of this invention have asymmetric carbon atoms within their structure and consequently that they may exist in different stereochemical optical isomeric forms. More particularly, when an alkylgroup is present in the 4-position of the dioxolanenucleus, the carbon atom to which it is attached and the carbon atom in the 2-position of the dioxolanenucleus are asymmetric. The stereochemical optical isomers of compounds of formula (I) may be separated and isolated by methods which are known to those skilled in the art. These isomers are intended to be within the scope of the present invention.

The compounds of formula (I) and the acid addition salts thereof are useful agents in combatting fungi and bacteria. The compounds of this invention are therefore valuable in the treatment of plants, animals and human beings suffering from pathogenic microorganisms and in the destruction of microorganism on materials.

The compounds of the present invention are very potent agricultural fungicides. They are very active against a wide variety of fungi such as those responsible for the occurrence of powdery mildew on different plant species, e.g. Erysiphe graminis, Erysiphe polygoni, Erysiphe cichoracearum, Erysiphe polyphaga, Podosphaera leuchotricha, Sphaerotheca pannosa, Sphaerotheca mors-uvae and Uncinula necator, and other fungi, such as Venturia inaequalis, Colletotrichum lindemuthianum, Fusarium oxysporum, Alternaria tenuis, Thielaviopsis basicola, Helminthosporium gramineum and Penicillium digitatum.

They are especially useful in view of their prophylactic as well as curative and systemic action. Their potent antifungal action against phytopathogenic fungi is more clearly illustrated by the results obtained in the following experiments.

In several of these experiments the compound 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole, (I-a), was used as a representative member of the compounds of formula (I).



(I-a)

It is understood that the compounds for which experimental test results are presented are not given for the purpose of limiting the invention thereto but only to exemplify the strong antifungal activity of the compounds of formula (I).

A. Prophylactic action of compounds of formula (I) against Erysiphe cichoracearum on cucumber upon foliar treatment.

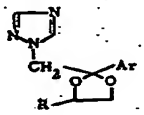
Young cucumber plants, about 10 days old, were sprayed with an aqueous solution containing 250, 100 or 10 ppm of the compound to be tested while controls were

kept untreated. After drying of the plants, artificial infection with spores of Erysiphe cichoracearum was carried out by slightly rubbing the plants with a heavily infected leaf. At the 15th. day after artificial infection the degree of fungal attack was evaluated by counting the number of spots per plants. The results given in table I are mean values for 2 plants and expressed according to the following score system.

0 = 0 spots per plant.
1 = 1 to 5 spots per plant.
2 = 6 to 10 spots per plant.
3 = more than 10 spots per plant.

TABLE I

Prophylactic action of compounds (I) against Erysiphe cichoracearum on cucumber plants upon foliar treatment



Ar	R	Base or Salt form	Antifungal score		
			250 ppm	100 ppm	10 ppm
2,4-$(Cl)_2$-C_6H_3	H	base	—	0	0
C_6H_5	H	base	—	3	—
4-NO_2-C_6H_4	H	base	0	—	—
3-Cl-C_6H_4	H	base	—	2	—
2-Cl-C_6H_4	H	$(COOH)_2$	—	0	—
4-Br-C_6H_4	H	base	0	—	—
2-Br-C_6H_4	H	$(COOH)_2$	—	2	—
3-OCH_3-C_6H_4	H	$(COOH)_2$	1	—	—
2-CH_3-C_6H_4	H	$(COOH)_2$	0	—	—
4-F-C_6H_4	H	$(COOH)_2$	0	—	—
4-CH_3-C_6H_4	H	$(COOH)_2$	0	—	—
4-Cl-C_6H_4	H	$(COOH)_2.H_2O$	—	0	—
2-naphthyl	H	$(COOH)_2$	0	—	—
2,5-$(Cl)_2$-C_6H_3	H	$(COOH)_2$	—	0	—
4-CN-C_6H_4	H	$(COOH)_2$	0	—	—
3,4-$(Cl)_2$-C_6H_3	H	$(COOH)_2$	—	3	—
2-OCH_3-C_6H_4	H	$(COOH)_2$	1	—	—
2-thienyl	H	$(COOH)_2$	—	2	—

TABLE I (Continued)

Ar	R	Base or Salt form	Antifungal score 250 ppm	100 ppm	10 ppm
2-fluorenyl	H	base	0	—	—
5–Cl–2–thienyl	H	base	—	2	—
3–Br, 4–CH_3–C_6H_3	H	base	0	—	—
2–CH_3, 4–Br–C_6H_3	H	base	—	2	—
2–CH_3, 4–Cl–C_6H_3	H	base	0	—	—
3–Br–C_6H_4	H	base	2	—	—
4–I–C_6H_4	H	$(COOH)_2$	0	—	—
3,5–$(Cl)_2$–C_6H_3	H	$(COOH)_2$	—	2	—
2,3–$(Cl)_2$–C_6H_3	H	$(COOH)_2$	0	—	—
3–NO_2–C_6H_4	H	base	1	—	—
2,4–$(Br)_2$–C_6H_3	H	$(COOH)_2$	—	1	—
2,4,5–$(Cl)_3$–C_6H_2	H	$(COOH)_2$	0	—	—
2–Cl, 4–OCH_3–C_6H_3	H	$(COOH)_2$	—	2	—
2,4–$(Cl)_2$–C_6H_3	CH_3	HNO_3	0	—	—
2,4–$(Cl)_2$–C_6H_3	C_2H_5	HNO_3	—	0	0
2,4–$(Cl)_2$–C_6H_3	nC_3H_7	HNO_3	—	0	0
2,4–$(Cl)_2$–C_6H_3	nC_4H_9	1 1/2$(COOH)_2$	—	2	—
2,4–$(Cl)_2$–C_6H_3	nC_5H_{11}	HNO_3	—	0	0
2,4–$(Cl)_2$–C_6H_3	nC_6H_{13}	HNO_3	0	—	—
2,4–$(Cl)_2$–C_6H_3	nC_7H_{15}	HNO_3	—	2	—
2,4–$(Cl)_2$–C_6H_3	nC_8H_{17}	HNO_3	0	—	—

A.1 Prophylactic action against Erysiphe polyphaga on cucumber upon foliar treatment.

Young cucumber plants in the one-leaf stage were sprayed with an aqueous solution containing 500, 250 or 125 ppm of (I-a) while controls were kept untreated. Artificial infection with spores of Erysiphe polyphaga was carried out by slightly rubbing the plants with a heavily infected leaf on the 4th., 6th. or 8th. day after treatment. At the 18th. and 34th. day after treatment, the percentage of leaf surface attacked by the fungus was determined separately for the infected leaves and for the newly developed leaves. The results given in Table I.1 are mean values for 5 plants and expressed in percent attack as compared to untreated.

TABLE I.1

Prophylactic activity of (I-a) against Erysiphe polyphaga on cucumber upon foliar treatment

Date of evaluation	18 days after treatment						34 days after treatment					
Infected at stated day after treatment	4		6		8		4		6		8	
Infected leaves (a) or newly developed leaves (b)	a	b	a	b	a	b	a	b	a	b	a	b
Concentr. of (I-a) in spray solution												
Untreated	100	100	100	100	100	100	100	100	100	100	100	100
500 ppm	0	0	0	0	0	0	0	0	0	0	0	0
250 ppm	0	0	0	0	0	0	0	0	0	0	0	0
125 ppm	0	0	0	0	0	0	0	0	0	0	0	0

B. Prophylactic action against Erysiphe graminis on barley upon soil treatment.

Barley plants were treated by watering with 100 ml. per plant of an aqueous solution containing 1,000, 100 or 10 ppm of (I-a). Controls received the same volume of the solution containing no (I-a). Natural infection, which normally occurs when the plants are held in the glass-house in the vicinity of infected plants; was evaluated 16 days after treatment by counting the number of spots on the leaves. Per object 5 plants were used and the results in Table II are mean values expressed in percent attack as compared to the controls.

TABLE II

Prophylactic action of (I-a) against Erysiphe graminis on barley upon soil treatment

Dose in mg. (I-a) per plant	% attack versus control
Control	100
100 mg	0
10 mg	0
1 mg	53

C. Curative action against Erysiphe graminis on barley upon foliar treatment. Barley plants attacked by Erysiphe graminis were sprayed with an aqueous solution containing (I-a) at the indicated concentration. On the 16th. day after treatment the number of spots per plant was determined. Per object 5 plants were used and the results given in Table III are mean values expressed in percent attack as compared to control.

TABLE III

Curative action of (I-a) against Erysiphe graminis on barley upon foliar treatment

Concentration of (I-a) in the spray-solution	% attack compared to control
0	100
1000 ppm	0
100 ppm	1.5
10 ppm	25

D. Prophylactic action of (I-a) against Podosphaera leuchotricha on apple seedlings upon spraying.
Apple seedlings, one year old, were sprayed with an aqueous solution containing (I-a) at the indicated concentration. The plants were artificially infected as described in test "A" with spores of Podosphaera leuchotricha 1 day after treatment and incubated for 36 hours. The degree of fungal attack was evaluated 25 days after treatment by counting the number of spots. Per object 2 plants were used and the results given in Table IV are mean values expressed in percent attack as compared to control.

TABLE IV

Propylactic action of (I-a) against Podosphaera leucotricha on apple seedlings upon spraying

Concentration of (I-a) in spraying solution	% attack compared to control
0	100
100 ppm	0
0 ppm	6

E. Activity against Thielaviopsis sp.

Slides of potato and leek, 5 mm. thick, were dipped in an aqueous test solution, containing (I-a) at the stated concentration. After dipping, the slides were placed on filter paper in a large plastic tray and the tray was covered with glass. Artificial infection was carried out at the day of treatment by spraying the slides with a concentrated suspension of spores of Thielaviopsis sp. and the slides were incubated at room temperature.

Fungal growth on the slides was evaluated 6 days after treatment by estimating the surface attacked by the fungus. The results given in Table V are expressed in percent attack as compared to the control.

TABLE V

Activity of (I-a) against Thielaviopsis sp.

Concentration of (I-a) in the test-solution in ppm	% attack compared to control	
	Potato	Leek
0	100	100
1 000	0	0
100	0	0
10	0	42.8
1	11	100

The compounds of formula (I) are also very active against a wide variety of fungi which are pathogenic to human beings and animals. For example they are active against fungi such as Microsporum canis, Trichophyton mentaprophytes, Trichophyton rubrum, Aspergillus fumigatus, Phialophora verucosa, Cryptococcus neoformans, Candida albicans, and Candida tropicalis. The excellent activity against Candida albicans is more clearly demonstrated by the results obtained in the following experiments.

F. Activity of (I-a) against crop candidosis in turkeys.

Young turkeys (14 days old) were artificially infected by gavage into the crop of a suspension containing 4.10^6 C.F.U. (colony forming units) of Candida albicans. After the infection the animals received either their normal diet (control group) or a medicated food containing 125 ppm of (I-a). Two weeks thereafter all turkeys were sacrificed, cultures were made of the crop, and the number of candida colonies per gram of crop were counted.

The results are summarized in Table VI.

TABLE VI

Number of colonies of Candida albicans per gram of crop in turkeys treated with (I-a) — (125 ppm) or placebo

Treatment	Number of the animal	Number of Candida colonies per gram crop
Controls	1	3,520,000
	2	848,700
	3	3,132,000
	4	1,909,000
(I-a) (125 ppm)	1	0
	2	247,200
	3	6,742

As is shown by the results in Table VI, (I-a) at the 125 ppm level is highly effective against crop candidosis as compared to the corresponding controls.

G. Activity of (I-a) against vaginal candidosis in rats.

Female rats of 100 g. body weight were ovariectomized and hysterectomized. About three weeks thereafter all animals received a weekly subcutaneous injection of 100 mg. oestradiol undecylate and were infected intravaginally with a suspension containing 8.10^5 C.F.U. of Candida albicans.

Groups of four rats were then orally treated for 14 consecutive days with either solvent (PEG 200) or (I-a). The administered dose of the compound was 40 mg/kg orally. Vaginal smears were taken from all animals at the end of the treatment period (i.e. 14 days), cultivated on Sabouraud agar medium containing Penicillin (20 I.U./ml) and Streptomycin (40 μg/ml), and the number of Candida colonies were counted thereafter.

Table VII summarizes the results obtained with (I-a) against vaginal candidosis in rats.

TABLE VII

Number of animals per culture score

Treatment	Number of animals	Day after treatment	Culture score*)				
			0	1	2	3	4
Controls (PEG 200)	4	14	0	0	0	1	3
(I-a) (40 mg/kg orally)	4	14	3	1	0	0	0

*) culture score: 0 = no growth
1 = 1-25 colonies
2 = 26-100 colonies
3 = >100 colonies
4 = inumerable colonies

As is apparent from the results in Table VII, (I-a) is a very potent agent against vaginal candidosis in rats.

H. Activity of (I-a) against systemic candidosis in guinea pigs.
Adult male guinea pigs were intravenously infected with Candida albicans, which induces a general systemic candidosis. Afterwards groups of 7 guinea pigs were orally treated for 14 consecutive days with either solvent (PEG 200) or (I-a). The dose used was 40 mg/kg. body weight.
Four days after the last treatment day, all animals were sacrificed, the kidneys removed, cultivated on Sabouraud agar medium containing Penicillin (20 U.I./ml) and Streptomycin (40 μg/ml) and the number of isolated Candida albicans colonies per gram kidney were counted. Table VIII shows the detailed results obtained with (I-a) against a systemic deep mycosis in guinea pigs.

TABLE VIII

Treatment	Number of the animal	Number of Candida colonies per gram kidney
Controls (PEG 200)	1	182
	2	2,838
	3	25,220
	4	385
	5	19,800
	6	113
	7	345
(I-a) (40 mg/kg) orally)	1	0
	2	18
	3	0
	4	0
	5	0
	6	53
	7	0

From the results in Table VIII is may be concluded that (I-a) is an extremely potent agent against a systemic deep mycosis in guinea pigs.

Apart from their antimicrobial effects, the compounds of formula (I) possess valuable plant growth regulating properties. Depending on different factors such as the species of the plants under treatment and the dose of active ingredient administered, the observed effect may be growth stimulation as well as growth inhibition. As such the compounds of this invention are useful as plant growth regulators. More particularly they may be used as plant growth inhibitors or retardants, especially as inhibitors of sucker growth, e.g., on tobacco plants. Under certain circumstances they may however also be used as plant growth stimulators.

The plant growth regulating properties of the compounds of formula (I), which are naturally intended to be within the scope of this invention, are more clearly illustrated by the results obtained in the following experiments, wherein the compound (I-a) was used as a representative member of the compounds of this invention. The results obtained with (I-a) are not given for the purpose of limiting

the invention thereto but only in order to exemplify the useful plant growth regulating properties of all the compounds within the scope of formula (I).

I. Growth regulating effect on tomato plants upon soil treatment.

Young tomato plants 3.5 to 4 cm. high were planted in separate pots. Each pot was watered with a test solution containing the indicated amount of (I-a). Growth was evaluated by determining the length and the weight of the plants 28 days after treatment.

The results given in Table IX are mean values of five plants expressed in percent as compared to the control plants.

TABLE IX

Growth regulating effect of (I-a) on tomato plants upon soil treatment

Dose of (I-a) in mg/plant	Length of plants in % compared to control	Weight of plants in % compared to control
none	100	100
10	114	118
1	127	134
0.1	122	116

J. Growth regulating effect on barley upon foliar treatment.

Young barley plants in the 3—4 leaf stage were sprayed with a test solution containing (I-a) in the indicated concentration. The effect on the growth of the plants is evaluated 24 days after treatment by determining the weight of the plants. The results given in Table X are mean values of ten plants expressed in percent as compared to the controls.

TABLE X

Growth regulating effect of (I-a) on barley upon foliar treatment

Conc. of (I-a) in test solution in ppm	Average weight of plants in percent of control
none	100
125	126
60	116

K. Sucker growth control on tobacco plants.

Tobacco plants, var. "Xanthi" were raised in the greenhouse and topped at the early button stage.

After 5 days, foliar spray treatment with an aqueous suspension of compound (I-a) at rates equivalent of 3 and 1.5 kg a.i./ha was carried out.

Each treatment was replicated 3 times. 12 Days after application, the subsequent sucker growth was assessed in comparison to the topped and untreated check plants.

The recorded reductions of sucker growth were 100% at the 3.0 kg/ha rate and 90% at 1.5kg/ha.

L. Growth inhibition on soybean plants.
Soybean plants, var. "Hark" were grown in pots in the growth chamber at 23°C, 20 000 Lux and a daylength of 14 hours. After the 3rd, trifoliate leaf had unfolded, the plants were sprayed with an aqueous suspension of compound (I-a) at concentrations of 1000, 500, 100 and 50 ppm active ingredient.
The % growth inhibition of the treated plants in comparison to the check was assessed after 14 days.
The following results were obtained:

Treatment		% growth inhibition
(I-a)	1000 ppm a.i.	70%
	500 ppm a.i.	40%
	100 ppm a.i.	25%
	50 ppm a.i.	0%
check		0%

At the concentration of 1000 ppm, a more intensive green colour of the foliage was observed.

In view of the aforementioned antifungal, antibacterial and growth-regulating activities the present invention also provides valuable compositions comprising the ketals of formula (I) or the acid addition salts thereof as the active ingredient in a solvent or a solid, semi-solid or liquid diluent or carrier, and, in addition, it provides an effective method of combatting fungus or bacterial growth by the use of an effective antifungal or antibacterial amount of such ketals (I) or salts thereof.
The compounds of the present invention can be used in suitable solvents or diluents, in the form of emulsions, suspensions, dispersions or ointments, on suitable solid or semi-solid carrier substances, in ordinary or synthetic soaps, detergents or dispersion media, if desired, together with other compounds having arachnicidal, insecticidal, ovicidal, fungicidal and/or bactericidal effects, or together with inactive additives.

Solid carrier substances which are suitable for the preparation of compositions in powder form include various inert, porous and pulverous distributing agents of inorganic or organic nature, such as, tricalcium phosphate, calcium carbonate, in the form of prepared chalk or ground limestone, kaolin, bole, bentonite, talcum, kieselguhr and boric acid; powdered cork, sawdust, or other fine pulverous materials of vegetable origin.

The active ingredient is mixed with these carrier substances, for example, by being ground therewith; alternatively, the inert carrier substance is impregnated with a solution of the active component in a readily volatile solvent and the solvent is thereafter eliminated by heating or by filtering with suction at reduced pressure. By adding wetting and/or dispersing agents, such pulverous preparations can also be made readily wettable with water, so that suspensions are obtained.

Inert solvents used for the production of liquid preparations should preferably not be readily inflammable and should be as far as possible odorless and as far as possible non-toxic to warm-blooded animals or plants in the relevant surroundings. Solvents suitable for this purpose are high-boiling oils, for example, of vegetable origin, and lower-boiling solvents with a flash point of at least 30°C., such as, for example, polyethylene glycol, isopropanol, dimethylsulfoxide, hydrogenated naphthalenes and alkylated naphthalenes. It is, of course, also possible to use mixtures of solvents. Solutions may be prepared in the usual way, if necessary, with the assistance of solution promoters. Other liquid forms which may be used consist of emulsions or suspensions of the active compound in water or suitable inert solvents, or concentrates for preparing such emulsions, which may be directly adjusted to the required concentration. For this purpose, the active ingredient is, for example, mixed with a dispersing or emulsifying agent. The active component may also be dissolved or dispersed in a suitable inert solvent and mixed simultaneously or subsequently with a dispersing or emulsifying agent.

It is also possible to use semi-solid carrier substances of a cream ointment, paste or waxlike nature, into which the active component may be incorporated, if necessary, with the aid of a solution promoter and/or emulsifier. Vaseline and other cream bases are examples of semi-solid carrier substances.

Furthermore, it is possible for the active component to be used in the form of an aerosol. For this purpose, the active component is dissolved or dispersed, if necessary, with the aid of suitable inert solvents as carrier liquids, such as difluorodichloromethane, which at atmospheric pressure boils at a temperature lower than room temperature, or in other volatile solvents. In this way, solutions under pressure are obtained which, when sprayed, yield aerosols which are particularly suitable for controlling or combatting fungi and bacteria, e.g., in closed chambers and storage rooms, and for application to vegetation for the eradication or for the prevention of infections by fungi or bacteria.

The compounds and compositions of the invention may be applied by conventional methods. For example, a fungus or bacterial growth or a material to be treated or the be protected against attack by fungus or bacterium may be treated with the subject compounds and the compositions thereof by dusting, sprinkling, spraying, brushing, dipping, smearing, impregnating or by other suitable means.

When the compounds of the invention are employed in combination with suitable carriers, e.g., in solution, suspension, dust, powder, ointment or emulsion form, a high activity over a very high range of dilution is observed. For example, concentrations of the active ingredient ranging from 0.1 to 10 percent by weight, based on the weight of compositions employed, have been found effective in combatting fungi or bacteria. Of course, higher concentrations may also be employed as warranted by the particular situation.

The following examples are intended to illustrate, but not to limit, the scope of the present invention. Unless otherwise stated, all parts are by weight.

Preparation I

A stirred and cooled (0°C) solution of 30 parts of 1-(4-amino-2-methoxyphenyl)ethanone in 360 parts of a concentrated hydrochloric acid solution, 75 parts of water and 30 parts of acetic acid was diazotated with a solution of 17.25 parts of sodium nitrite in 200 parts of water. After stirring for 30 minutes at 0°C, the whole was poured onto a solution of 30 parts of copper (I) chloride in 240 parts of a concentrated hydrochloric acid solution while stirring. The mixture was heated for 1 hour at 60°C. After cooling to room temperature, the product was extracted twice with 2,2'-oxybispropane. The combined extracts were washed successively with water, a diluted sodium hydroxide solution and again twice with water, dried, filtered and evaporated, yielding 28 parts (76%) of 1-(4-chloro-2-methoxyphenyl)ethanone;
m.p. 55°C.

Preparation II

3 Parts of 4-methylbenzenesulfonic acid and 225 parts of benzene were added to a stirred mixture of 78.8 parts of 2-bromo-1-(4-bromo-2-methylphenyl)-1-ethanone and 200 parts of butanol. 33.5 Parts of 1,2-ethanediol were then added dropwise thereto. Upon completion, stirring was continued overnight at a reflux temperature with a water-separator. The reaction mixture was evaporated and the residue was dissolved in 2,2'-oxybispropane. The solution was stirred with 15 parts of a concentrated sodium hydroxide solution. The layers were separated and the aqueous phase was extracted with 2,2'-oxybispropane. The combined organic layers were washed with water (till neutralization), dried, filtered and evaporated. The solid residue was crystallized from methanol, yielding 30.5 parts of 2-(bromomethyl)-2-(4-bromo-2-methylphenyl)-1,3-dioxane;
mp. 86°C.

Preparation III

Following the procedure of Preparation II but using an equivalent amount of an appropriate 1-aryl-2-bromo-1-ethanone in place of the 2-bromo-1-(4-bromo-2-methylphenyl)-1-ethanone used therein the following 2-aryl-2-bromomethyl-1,3-dioxolanes were prepared:
4-[2-(bromomethyl)-1,3-dioxolan-2-yl]benzonitrile;
mp. 92.4°C; and
2-(bromomethyl)-2-(2-naphthalenyl)-1,3-dioxolane;
mp. 64°C.

Preparation IV

57 Parts of 1-(5-chloro-2-thienyl)-1-ethanone were dissolved in 220 parts of 1,2-ethanediol at 50°C. While stirring, 64 parts of bromine were added dropwise, during a 1 hour-period, without external heating. After stirring for 1 hour at room temperature, 4 parts of 4-methylbenzenesulfonic acid and 360 parts of benzene were added. The whole was stirred and refluxed overnight with water-separator. The reaction mixture was evaporated and the residue was taken up in 2,2'-oxybispropane. The resulting solution was washed successively once with a dilute sodium hydroxide solution and three times with water, dried, filtered and evaporated. The residue was distilled, yielding 73.3 parts (64.5%) of 2-(bromomethyl)-2-(5-chloro-2-thienyl)-1,3-dioxolane; bp. 125—127°C at 0.1 mm pressure.

Preparation V

Following the procedure of Preparation IV but using therein an equivalent amount of an appropriate 1-aryl-1-ethanone in place of the 1-(5-chloro-2-thienyl)-1-ethanone used therein, the following 2-aryl-2-(bromomethyl)-1,3-dioxolanes were prepared:
2-bromomethyl)-2-(9H-fluoren-2-yl)-1,3-dioxolane; mp. 90°C.;
2-(bromomethyl)-2-(3-bromo-4-methylphenyl)-1,3-dioxolane; bp. 126—130°C. at 0.1 mm pressure;
2-(bromomethyl)-2-(4-iodophenyl)-1,3-dioxolane; mp. 74°C.;
2-(bromomethyl)-2-(4-chloro-2-methoxyphenyl)-1,3-dioxolane; mp. 110°C.; and
2-(bromomethyl)-2-(2,4-dibromophenyl)-1,3-dioxolane; mp. 96°C.

Example I.

A. 6.9 Parts of 1H-1,2,4-triazole in 150 parts of dimethylformamide were added to a stirred solution of 2.3 parts of sodium in 120 parts of methanol. The methanol was removed at normal pressure until the internal temperature of 130°C was reached. Then, 25 parts of 2-(bromomethyl)-2-(2,4-dichlorophenyl)-1,3-dioxolane were added. The reaction mixture was stirred and refluxed for 3 hours. It was allowed to cool to room temperature and poured onto water. The precipitated product was filtered off and crystallized from diisopropylether (activated charcoal), yielding 12 parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 109.9°C.

B. 6 Parts of 1-[2-(2,4-dichlorophenyl)-1,3,-dioxolan-2-ylmethyl]-1H-1,2,4-triazole were converted into the nitrate salt in 2,2'-oxybispropane. After cooling, the salt was filtered off and crystallized twice from 2-propanone, yielding 3 parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole nitrate; mp. 172.7°C.

C. 6 Parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole were converted into the sulfate salt in 2,2'-oxybispropane. The sulfate salt so-formed was filtered off and crystallized from 2-propanol. The product was filtered off and recrystallized from ethanol (activated charcoal), yielding, after drying, 6 parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole sulfate; mp. 207.1°C.

Example II.

6.9 Parts of 1H-1,2,4-triazole and 2 parts of sodium iodide in 100 parts of N,N-dimethylformamide were added to a stirred solution of 2.3 parts of sodium in 80 parts of methanol. The methanol was removed at normal pressure until the internal temperature of 130°C was reached. Then, 34.4 parts of 2-(bromomethyl)-2-(2,4-dichlorophenyl)-4-methyl-1,3-dioxolane were added and the whole was stirred and refluxed for 3 hours. The reaction mixture was poured onto water and the product was extracted twice with diisopropyl-ether. The extract was washed with water and an excess of concentrated nitric acid solution was added. The crude nitrate salt was filtered off and crystallized from a mixture of 2-propanol and diisopropylether, yielding 15 parts of 1-[2-(2,4-dichlorophenyl)-4-methyl-1,3-dioxolane-2-ylmethyl]-1H-1,2,4-triazole nitrate; mp. 137.8°C.

Example III.

8.3 Parts of 1H-1,2,4-triazole were added to a stirred sodium methoxide solution, prepared starting from 2.8 parts of sodium in 48 parts of methanol. After stirring for 30 minutes at room temperature, 135 parts of N,N-dimethyl-formamide were added and the methanol was evaporated. Then a mixture of 24.3 parts of 2-(bromomethyl)-2-phenyl-1,3-dioxolane and 3 parts of potassium iodide was added,

and the whole was stirred and refluxed for 3 hours. The reaction mixture was cooled to room temperature and poured onto water. Upon scratching, the product was precipitated. It was sucked off, washed with water, dried and crystallized from a mixture of ethanol and 2,2'-oxybispropane (1:5 by volume), yielding 10.9 parts (43.7%) of 1-(2-phenyl-1,3-dioxolan-2-ylmethyl)-1H-1,2,4-triazole; mp. 127.3°C.

Example IV.

Following the procedure of Example III but using an equivalent amount of an appropriate 2-aryl-2-(bromomethyl)-1,3-dioxolane in place of the 2-(bromomethyl)-2-phenyl-1,3-dioxolane used therein, the following 1,2,4-triazoles were obtained:
1-[2-(4-nitrophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 160.1°C.;
1-[2-(3-chlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 113.9°C.;
1-[2-(4-bromophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 135.9°C;
1-[2-(3-methylphenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 105.4°C.;
1-[2-(3-bromophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 115.4°C.; and
1-[2-(3-nitrophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole; mp. 154.1°C.

Example V.

4.9 Parts of 1H-1,2,4-triazole were added to a stirred sodium methoxide solution, prepared starting from 1.6 parts of sodium in 48 parts of methanol. After stirring for 1 hour at room temperature, 135 parts of N,N-dimethyl-formamide were added. The methanol was distilled off at normal pressure until an internal temperature of 130°C was reached. Then, 17.4 parts of 2-(bromomethyl)-2-(2,3,4-trichlorophenyl)-1,3-dioxolane and 3 parts of potassium iodide were successively added. The whole was stirred and refluxed overnight. After cooling to room temperature, the reaction mixture was poured onto water. Upon scratching, the product was precipitated, filtered off and washed with water. The product, dissolved in trichloromethane, was purified by column-chromatography over silicagel, using a mixture of trichloromethane and 5% of methanol as eluent. The pure fractions were collected and the eluent was evaporated. The residue was crystallized from a mixture of 2,2'-oxybispropane and methanol (9:1 by volume), yielding 9.3 parts (55.5%) of 1-[2-(2,3,4-trichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole, mp. 181.4°C.

Example VI.

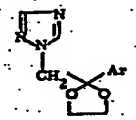
Following the procedure of Example V and using equivalent amounts of the appropriate starting materials the following 1,2,4-triazoles were prepared:
1 - [2 - (9H - fluoren - 2 - yl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole; mp. 186.8°C;
1 - [2 - (5 - chloro - 2 - thienyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole; mp. 117.4°C.;
1 - [2 - (3 - bromo - 4 - methylphenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4-triazole; mp. 120.7°C.;
1 - [2 - (4 - bromo - 2 - methylphenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4-triazole; mp 148.1°C.; and
1 - [2 - (4 - chloro - 2 - methylphenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4-triazole; mp. 147.9°C.

Example VI.

A mixture of 8.3 parts of 1H-1,2,4-triazole and 135 parts of N,N-dimethylformamide was added to a stirred sodium methoxide solution, prepared starting from 2.8 parts of sodium in 56 parts of methanol. The methanol was removed at normal pressure until an internal temperature of 130°C was reached. A mixture of 27.8 parts of 2-(bromomethyl)-2-(2-chlorophenyl)-1,3-dioxolane and 3 parts of potassium iodide was then added. The whole was stirred and refluxed for 6 hours. The reaction mixture was allowed to cool to room temperature, poured onto water and the product was extracted three times with 1,1'-oxybisethane. The combined extracts were washed twice with water, dried, filtered and evaporated. The residue was converted into the ethanedioate salt in 4-methyl-2-pentanone. The salt was filtered off and crystallized from 4-methyl-2-pentanone, yielding 16 parts of 1-[2-(2-chlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole ethanedioate; mp. 156.5°C.

Example VII.

Following the procedure of Example VI but using equivalent amounts of the appropriate starting materials, the following 1,2,4-triazole ethanedioate salts were prepared:



Ar	Acid salt	melting point
2-Br—C_6H_4	$(COOH)_2$	172.1°C.
3-OCH_3—C_6H_4	$(COOH)_2$	155.6°C.
2-CH_3—C_6H_4	$(COOH)_2$	177.1°C.
4-F—C_6H_4	$(COOH)_2$	185.5°C.
4-CH_3—C_6H_4	$(COOH)_2$	151.2°C.
4-Cl—C_6H_4	$(COOH)_2 \cdot H_2O$	169.1°C.
4-OCH_3—C_6H_4	$(COOH)_2$	187.1°C.
2-naphthalenyl	$(COOH)_2$	175°C.
2,5-$(Cl)_2$—C_6H_3	$(COOH)_2$	173.7°C.
4-CN—C_6H_4	$(COOH)_2$	186.3°C.
3,4-$(Cl)_2$—C_6H_3	$(COOH)_2$	182.2°C.
2-thienyl	$(COOH)_2$	144.5°C.
2,4-$(Br)_2$—C_6H_3	$(COOH)_2$	190.3°C.

Example VIII.

6.9 Parts of 1H-1,2,4-triazole were added to a stirred sodium methoxide solution, prepared starting from 2.3 parts of sodium in 48 parts of methanol. After stirring for 30 minutes at room temperature, 135 parts of N,N-dimethylformamide were added. The methanol was distilled off at normal pressure until an internal temperature of 130°C was reached. Then, 3 parts of potassium iodide and 16.4 parts of 2-(bromomethyl)-2-(*o*-methoxyphenyl)-1,3-dioxolane were added successively. The whole was stirred and refluxed for 18 hours. After cooling to room temperature, the reaction mixture was poured onto water and the resulting solution was extracted three times with trichloromethane. The combined extracts were washed four times with water, dried, filtered and evaporated. The residue was purified by column-chromatography over silicagel, using a mixture of trichloromethane and 5% of methanol as eluent. The pure fractions were collected and the eluent was evaporated. The residue was converted into the ethanedioate salt in 4-methyl-2-pentanone. The salt was filtered off and crystallized from a mixture of 2-propanone and 2,2'-oxybispropane (2:1 by volume), yielding 5.5 parts (26%) of 1-[2-(-methoxy-phenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole ethanedioate; mp. 166.4°C.

Example IX.

Following the procedure of Example VIII but using equivalent amounts of the appropriate starting materials, the following 1,2,4-triazole ethandioate salts were prepared:

1 - [2 - (4 - iodophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole ethanedioate; mp. 169.8°C.;

1 - [2 - (3,5 - dichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole ethanedioate; mp. 204.4°C.;

1 - [2 - (2,3 - dichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole ethanedioate; mp. 188.4°C;
1 - [2 - (4 - chloro - 2 - methoxyphenyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole ethanedioate; mp. 173.2°C.;
1 - [2 - (2,4,5 - trichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole ethanedioate; mp. 178.4°C.; and
1 - [2 - (2 - chloro - 4 - methoxyphenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole ethanedioate; mp. 188.2°C.

Example X.

4.2 Parts of a sodium hydride dispersion 78% were added portionwise to a stirred mixture of 9.5 parts of 1H-1,2,4-triazole and 225 parts of N,N-dimethylformamide. After stirring until foaming ceased, 16 parts of 2-(bromomethyl)-2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolane were added and stirring was continued for 5 hours at reflux temperature. The reaction mixture was cooled and poured onto water. The product was extracted three times with 2,2'-oxybispropane. The combined extracts were washed with water, dried, filtered and evaporated. The residue was purified by column-chromatography over silicagel using a mixture of trichloromethane and 2% of methanol as eluent. The first fraction was collected and the eluent was evaporated. The residue was converted into the nitrate salt in 2,2'-oxybispropane. The salt was filtered off and crystallized from a mixture of 2-propanone and petroleumether, yielding 8.2 parts (45%) of 1-[2 - (2,4 - dichlorophenyl) - 4 - propyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4-triazole nitrate; mp. 132.6°C.

Example XI.

11.5 Parts of 1H-1,2,4-triazole and 225 parts of N,N-dimethylformamide were added to a stirred sodium methoxide solution, prepared starting from 3.8 parts of sodium in 40 parts of methanol. The methanol was distilled off until an internal temperature of 150°C was reached. After the addition of 19 parts of 2-(bromomethyl)-2-(2,4-dichlorophenyl)-4-ethyl-1,3-dioxolane, the hole was stirred and refluxed for 4 hours. The reaction mixture was cooled and poured onto water. The product was extracted three times with 2,2'-oxybispropane. The combined extracts were washed with water, dried, filtered and evaporated. The residue was purified by column-chromatography over silicagel using a mixture of trichloromethane and 2% of methanol as eluent. The first fraction was collected and the eluent was evaporated. The residue was converted into the nitrate salt in 2,2'-oxybispropane. The salt was filtered off and recrystallized from a mixture of 4-methyl-2-pentanone and 2,2'-oxybispropane, yielding 10.5 parts (49%) of 1-[2-(2,4-dichlorophenyl)-4-ethyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole nitrate; mp. 119.8°C.

Example XII.

Following the procedure of Example XI but using equivalent amounts of the appropriate starting materials, the following 1,2,4-triazole acid addition salts were prepared:
1 - [4 - butyl - 2 - (2,4 - dichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole sesquiethanedioate; mp. 111.6°C.;
1 - [2 - (2,4 - dichlorophenyl) - 4 - pentyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole nitrate; mp. 130.3°C.;
1 - [2 - (2,4 - dichlorophenyl) - 4 - hexyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole nitrate; mp. 106.2°C.;
1 - [2 - (2,4 - dichlorophenyl) - 4 - heptyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole nitrate; mp. 96.8°C.; and
1 - [2 - (2,4 - dichlorophenyl) - 4 - octyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole nitrate; mp. 110.6°C.

Example XIII.

By repeating the procedure of Example I—A except that the 2-(bromomethyl)-2-(2,4-dichlorophenyl)-1,3-dioxolane used therein was replaced by an equivalent amount of an appropriate 2-(bromomethyl)-2-aryl-1,3-dioxolane, the following compounds of formula (I) were obtained respectively:
1 - [2 - (2,4,6 - trichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole;
1 - [2 - (2,6 - dichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H-1,2,4 - triazole;
1 - [2 - (2 - chloro - 4 - methylphenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4-triazole

Example XIV.

The procedure of Example II may be used to prepare compounds of formula (I) wherein Z is $—CH_2—CH(CH_3)—$ or $—CH(CH_3)—CH(CH_3)—$. Accordingly, by substituting therein an equivalent amount of an appropriate 2-aryl-2-(bromomethyl)-4-methyl-1,3-dioxolane or 2-aryl-2-(bromomethyl)-4,5-dimethyl-1,3-dioxolane, the following compounds are obtained respectively in the form of a nitrate salt:

1-(4-methyl-2-phenyl-1,3-dioxolan-2-ylmethyl)-1H-1,2,4-triazole;
1-[2-(4-chlorophenyl)-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole;
1 - [2 - (2 - chlorophenyl) - 4 - methyl - 1,3 - dioxolan - 2 - ylmethyl]-1H - 1,2,4 - triazole;
1 - [4 - methyl - 2 - (4 - methylphenyl) - 1,3 - dioxolan - 2 - ylmethyl]-1H - 1,2,4 - triazole;
1 - [2 - (4 - methoxyphenyl) - 4 - methyl - 1,3 - dioxolan - 2 - ylmethyl]-1H - 1,2,4 - triazole;
1 - [4,5 - dimethyl - 2 - (2,4 - dichlorophenyl) - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole;
1 - (4,5 - dimethyl - 2 - phenyl - 1,3 - dioxolan - 2 - ylmethyl]-1H - 1,2,4 - triazole; and
1 - [2 - (4 - chlorophenyl) - 4,5 - dimethyl - 1,3 - dioxolan - 2 - ylmethyl] - 1H - 1,2,4 - triazole.

Example XV.

The procedure set forth in Example I—A may be utilized to prepare those compounds of formula (I) wherein Z is $—CH_2—CH_2—CH_2—$. Accordingly, by substituting therein an equivalent quantity of an appropriate 2-aryl-2-(bromomethyl)-1,3-dioxane as starting material, the following are obtained respectively:

1-(2-phenyl-1,3-dioxan-2-ylmethyl)-1H-1,2,4-triazole;
1-[2-(2,4-dichlorophenyl)-1,3-dioxan-2-ylmethyl]-1H-1,2,4-triazole;
1-[2-(4-chlorophenyl)-1,3-dioxan-2-ylmethyl]-1H-1,2,4-triazole;
1-[2-(4-methylphenyl)-1,3-dioxan-2-ylmethyl]-1H-1,2,4-triazole;
1-[2-(4-methoxyphenyl)-1,3-dioxan-2-ylmethyl]-1H-1,2,4-triazole;
1-[2-(2-thienyl)-1,3-dioxan-2-ylmethyl]-1H-1,2,4-triazole; and
1-[2-(2-naphthyl)-1,3-dioxan-2-ylmethyl]-1H-1,2,4-triazole.

Example XVI.

The compositions according to this invention may be employed in those forms which are customarily used for fungus or bacteria control, for example, as suspensions, dusting powders, solutions or ointments. The following will further illustrate the invention, the parts being parts by weight unless otherwise specified:

(1) SUSPENSION:

1 kg. . . .	1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-yl-methyl]-1H-1,2,4-triazole
2 l. . . .	technical xylene
350 m. . . .	Surfactant
Water . . .	dilute to desired concentration to active ingredient

The 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole formed a stable aqueous suspension when dissolved in the xylene and emulsified by means of the surface active agent.

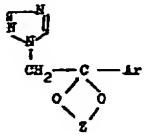
(2) DUSTING POWDER: 20 Parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole were ground with 360 parts of talcum in a ball mill, then 8 parts of olein were added and grinding was continued, and finally the mixture was mixed with 4 parts of slaked lime. The powder which was formed can be sprayed satisfactorily and has good adhesive power. It can be used for dusting or for plant protection purposes.

(3) SOLUTION: 5 Parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole were dissolved in 95 parts of alkylated naphthalene and used as a spray for the treatment of fungus-infected subjects or on walls, floors, or other objects to prevent infection by fungi.

(4) OINTMENT: 10 Parts of 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole were dissolved in a warm, liquefied mixture of 400 parts of polyethylene glycol 400 and 590 parts of polyethylene glycol 1500. The solution was stirred during cooling, and used as an ointment for treatment against fungi and bacteria.

WHAT WE CLAIM IS:—

1. A 1-(β-aryl)ethyl-1H-1,2,4-triazole ketal having the formula:



(I)

or the therapeutically active acid addition salts thereof, wherein Z is an alkylene group of the formula

$$-CH_2-CH_2-,\ -CH_2-CH_2-CH_2-,\ -CH(CH_3)-CH(CH_3)-\text{ or } -CH_2-CH(\text{alkyl})-,$$

wherein said alkyl group has from 1 to 10 carbon atoms; and Ar is a phenyl, thienyl, halothienyl, naphthyl or fluorenyl group, or a substituted phenyl group having from 1 to 3 substituents which are independently a halogen atom, a loweralkyl, loweralkoxy, cyano or nitro group.

2. 1-[2-(2,4-Dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof.

3. 1 - [2 - (2,4 - Dichlorophenyl)-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof.

4. 1 - [2 - (2,4-Dichlorophenyl)-4-ethyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof.

5. 1 - [2 - (2,4-Dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof.

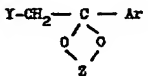
6. 1 - [2 - (2,4-Dichlorophenyl)-4-pentyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof.

7. A compound of formula (I) as claimed in claim 1 and other than those claimed in claims 2 to 6, substantially as hereinbefore described with reference to any one of the Examples.

8. A process for preparing a 1-(β-aryl)ethyl-1H-1,2,4-triazole ketal of formula (I) as claimed in claim 1, or a therapeutically active acid addition salt thereof, which process comprises reacting a metal salt of a compound of the formula

II

with a compound of the formula



(III)

wherein Y is a halogen atom and Ar and Z are as defined in claim 1, and, if desired, separating and isolating stereochemical optical isomers of the products thereof by known procedures, and further, if desired, preparing therapeutically active acid addition salts of said products.

9. A process as claimed in claim 8 wherein the reaction is carried out in a polar reaction-inert organic solvent at an elevated temperature.

10. A process as claimed in claim 8 or claim 9 wherein Y is a bromine atom.

11. A process for preparing 1-[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof, which comprises reacting 1H-1,2,4-triazole with 2-(bromomethyl)-2-(2,4-dichlorophenyl)-1,3-dioxolane and, if desired, preparing a therapeutically active acid addition salt thereof.

12. A process for preparing 1-[2-(2,4-dichlorophenyl)-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof, which comprises reacting 1H-1,2-triazole with 2-(bromomethyl)-2-(2,4-dichlorophenyl)-4-methyl-1,3-dioxolane, and, if desired, preparing a therapeutically active acid addition salt thereof.

13. A process for preparing 1-[2-(2,4-dichlorophenyl)-4-ethyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof, which comprises reacting 1H-1,2,4-triazole with 2-(bromomethyl)-2-(2,4-dichloro-

phenyl)-4-ethyl-1,3-dioxolane, and, if desired, preparing a therapeutically active acid addition salt thereof.

14. A process for preparing 1-[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof, which comprises reacting 1H-1,2-triazole with 2-(bromomethyl)-2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolane and, if desired, preparing a therapeutically active acid addition salt thereof.

15. A process for preparing 1-[2-(2,4-dichlorophenyl)-4-pentyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole or a therapeutically active acid addition salt thereof, which comprises reacting 1H-1,2,4-triazole with 2-(bromomethyl)-2-(2,4-dichlorophenyl)-4-pentyl-1,3-dioxolane, and, if desired, preparing a therapeutically active acid addition salt thereof.

16. A process for preparing a compound of formula (I) as claimed in claim 1 substantially as hereinbefore described.

17. A process for preparing a compound of formula (I) as claimed in claim 1 substantially as hereinafter described with reference to any one of the Examples I to XV.

18. A compound of formula (I) as claimed in claim 1 whenever prepared by a process as claimed in any one of claims 8 to 17.

19. A composition for combatting a fungus or a bacterium, or for regulating the growth of plants, which comprises an inert carrier material and as an active ingredient an effective amount of a compound of formula (I) as claimed in claim 1 or a therapeutically active acid addition salt thereof in admixture with a solvent, diluent or carrier therefor.

20. A composition as claimed in claim 19 wherein the compound of formula (I) is a compound as claimed in any one of claims 2 to 7, or claim 17.

21. A composition as claimed in claim 19 substantially as hereinbefore described.

22. A process for combatting or preventing a fungal or bacterial infection in a plant or in a non-human animal which process comprises treating the said plant or animal either prior to or after exposure to the said fungal or bacterial infection with a composition as claimed in claim 21.

23. A process for regulating the growth of a plant which process comprises treating the said plant with a composition as claimed in claim 21.

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